

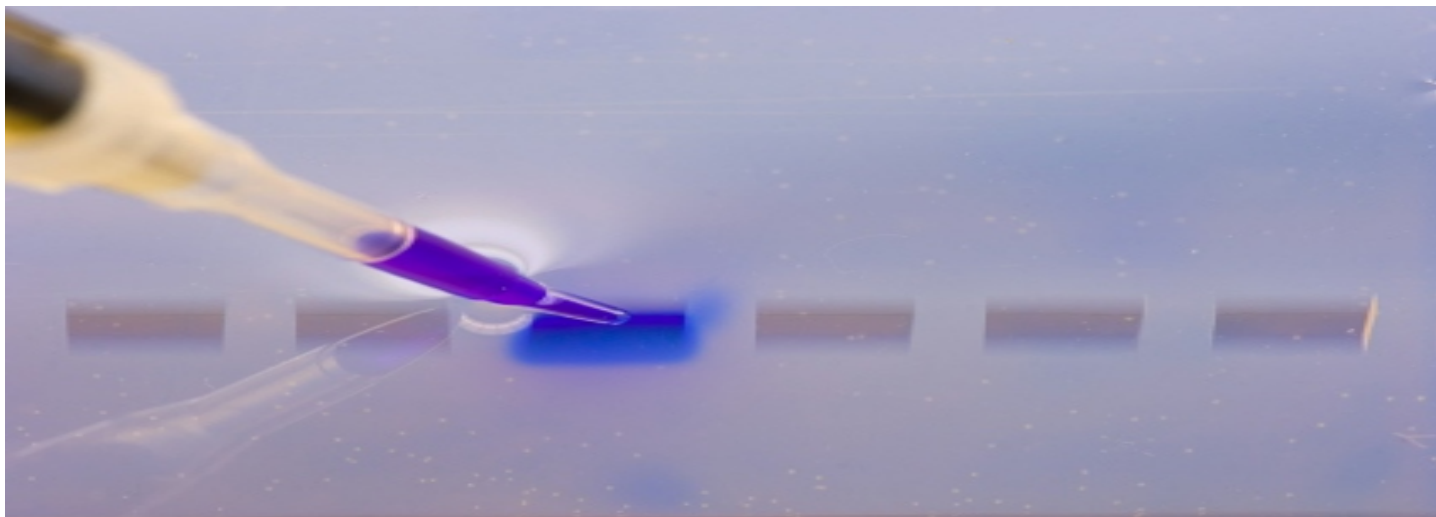
ROLE OF INTELLECTUAL PROPERTY IN BIOTECHNOLOGY



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The introduction of Biotechnology to mankind is the most valuable development till now. The proliferation began when the ancient Sumerian in the year 1750 B.C. first brewed beer by using yeast and other microorganisms. The further fission was catalyzed by the successors such as the Egyptians, Darwin, Pasteur, Mendel, Morgan, Fleming, Watson and Crick, Nirenberg, Boyer, Wilmut and is still continuing with the present time scientists. With the invention of many more techniques, processes, and products, biotech field has been explored at a very high pace.

INDUSTRY OVERVIEW

Indian Biotech Industry has just completed its 30th year. The year 1982 was the landmark year for the Biotech Industry in India when Government of India implemented the National Biotech Board [NBTB] and further Department of Biotechnology [DBT]. The Indian Biotech Industry contributes about 2 percent to India's GDP with turnover of around Rs.17, 400 crore. The Indian biotech industry has emerged on the global map with the strong asset of 3 million science graduates, 0.7 million postgraduates and 7000 PhDs. It employs 20, 000 Scientists, 45, 000 Assistants, and 1, 25000 Technicians and other staffs either directly or indirectly.

According to a report of BioSpectrum and ABLE the turnover of the Indian Biotech Industry is expected to rise up to Rs.45, 000 crore by 2015.

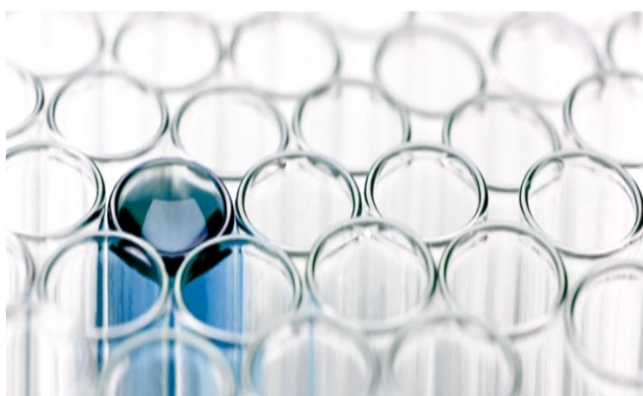
Indian Biotech Industry is:

- . Third largest in the Asian region;
- . Among top 12 biotech destinations in the world;
- . Ranked 12 for Phase II & III clinical trial study sites among the most active countries;
- . Second Largest vaccine manufacturer in the world; and
- . Fourth largest adopter of biotech crops in the World.

Indian Biotech Industry has strengths in biotech research that include fermentation based compounds, extraction of high quality products using plant and animal parts, recombinant DNA technology, vaccine production, plant breeding techniques, plant cell/tissue culture, bioprocess engineering, and use of cell/microbial culture techniques. There are about 362 registered biotech-based companies in India. Out of these, 60 are in the modern biotech sector.

MAJOR PLAYERS

Biotechnology Industry is largely dominated by companies serving both the pharmaceutical and biotechnology industries. Out of 362 biotechnology firms in India, 54% of the revenue comes from the top 20 players namely Biocon, Serum Institute of India, Panacea Biotec, Nuziveedu seeds, Reliance Life Sciences, Rasi Seeds, Mahyco, Transasia, Ankur Seeds, Syngene International, Bharat Biotech, Krishidhan Seeds, Shantha Biotech, Novozymes, Bharat Serum, Jubilant Life Sciences, Siro Clinpharm, Cadila, Indian Immunologicals, and Tulip Group.



BIOCON: First and leading Biotech Company in India.

SERUM INSTITUTE OF INDIA: World's largest producer of measles and DTP vaccine.

PANACEA BIOTECH: World class production of bacterial and viral vaccines.

WOCKHARDT: Biopharma powerhouse of India with 11 world class manufacturing plants in India.

SHANTHA BIOTECHNICS: It is known for its Hepatitis B vaccine, Streptokinase drug and Interferon alpha-2b. Shantha's hepatitis B vaccine became India's first recombinant product to be made indigenously in the healthcare sector. Today this vaccine is available in 52 countries and makes up 40% of UNICEF's supply.

MAHYCO MONSANTO: Worldwide famous for a number of Bt cotton hybrids.

CIPLA: Has introduced inexpensive generic antiretroviral drugs.

STRAND GENOMICS: With association of France's bioMerieux to develop diagnostic instruments for medical and industrial applications.



Apart from private companies, Government of India's subsidiaries also have major contribution in the development and proliferation of Biotech Industry in India. These Indian R&D bases have major impact and are working together with the Indian Biotech Companies.

Centre for Cellular & Molecular Biology (CCMB): Established in Hyderabad in 1981

International Centre for Genetic Engineering & Biotechnology (ICGEB): Established in Delhi in 1983

Institute of Microbial Technology (IMTECH): Established in Chandigarh in 1984

Department of Biotechnology (DBT): Established in 1986 under the Ministry of Science & Technology

National Institute of Immunology (NII): Established in New Delhi in 1987

National Centre for Biological Sciences (NCBS): Established in Bangalore in 1991

Centre for DNA Fingerprinting and Diagnostics (CDFD): Established in Hyderabad in 2003

BIOTECH CLUSTERS IN INDIA

The biotech companies are distributed in three major clusters across the country. The largest in terms of revenue generated is the Western Cluster (Ahmedabad, Aurangabad, Mumbai and Pune), followed by the Southern Cluster (Bangalore, Chennai and Hyderabad) and the Northern Cluster (Delhi, Gurgaon and Noida).

MAJOR SEGMENTS

According to reports, in FY 2010-11, exports stood at Rs.8, 852 crores and contributed to 51% of the total business with bio-pharma products currently contributing to 61.77% of the exports. Domestic business accounted for Rs.8, 397 crores. The key opportunity segments are: bio-pharmaceutical (vaccines, therapeutics, and diagnostics), bio-agri (transgenics, biofertilizers, biopesticides), bio-industry, bio-informatics and bio-services (R&D, clinical trials, and manufacturing on contract).

The Biotech Industry produces more than 200 new techniques of therapy and vaccines to cure diabetes, cancer, AIDS and other autoimmune diseases. The Indian Biotech Industry is divided into following comprehensive segments which include:

BIO PHARMA: It is the largest segment of the industry both in terms of domestic and export revenues. And, it contributes to 61.77% of the total business. The major products can be further categorized into Therapeutics, Diagnostics, and Vaccine. Vaccine business contributes more to this segment. Diagnostics business comprises majority of reagents and kits. Therapeutics business involves mainly insulin, Erythropoietin, Streptokinase and Interferons. Other products include Growth hormones, Granulocyte Stimulating Factor, Follicle Stimulating Factor, Blood Factor VIII, Tissue Plasmogen Activator and others.

BIO AGRI: This segment is one of the fastest growing sectors. And, it contributes to 14.38% of the total business. It can be segmented into: Hybrid seeds and transgenic crops, Biopesticides, & Biofertilizers. Genetically modified cotton or commonly known as Bt cotton constitutes major percentage share of the revenue in this sector. 97% of this sector's revenues come through the domestic route.



BIO INDUSTRIAL: Generating 3.63% percent of the total revenues of the biotechnology industry, it brought in Rs. 625 Crores in 2010-11. Although it accounts for a higher market share than Bioinformatics, but it was found to record the slowest growth compared to its counterparts. This sector of industry predominantly consists of enzyme manufacturing and marketing companies. These enzymes are mainly used in industries such as detergents, textiles, food, leather, paper and pharmaceuticals. In 2011, 76 percent of its revenue came from the domestic market.

BIO SERVICES: The Bioservices market is the second largest sector of the Indian Biotechnology Industry. The market's growth can be attributed to the fact that India has become a popular destination for clinical trial, contract research and manufacturing activities. Therefore, it is no surprise that BioServices accounted for over 18.82% of the total biotech business in 2010-11. Another statistical data to note is that only 8 percent of the BioServices revenue came from the domestic market.

BIO INFORMATICS: This is probably the smallest part of the current domestic biotechnology industry. However it is not a market to be underestimated; India is known for its strong IT base and it is due to this that India is sure to become a leading destination for work in the bioinformatics arena. There are around 35 companies in this space who are into core bioinformatics development, both in terms of developing the market and product while others are solely into marketing. Major players in this segment are Strand Genomics, Accelrys, GVK Biosciences, Molecular Connections, Tata Consultancy Services

BIO SUPPLIERS: With the biotechnology industry growing at a fast pace, its suppliers are also growing equally fast. Major suppliers include American, European and Indian companies with products as simple as test tubes and other consumables to high-end equipments. The market is currently dominated by MNCs that want to take advantage of the increased R&D investments by domestic biotechnology and pharmaceutical companies.

INTELLECTUAL PROPERTY

With the advent of newer technologies to diagnose diseases and to further discover new drugs to cure these diseases; the world's biotech industry are going through a period of fundamental revolution. The modern biotech Industry is just 40-50 years old but, it grew more and has witnessed major breakthrough in comparison to other industries. Discovery and Innovation are playing major role in the proliferation, utilization and development of Biotech Industry. Discovery of newer things encourages industries to innovate more efficient products and devices to keep up with the current challenges and market demands.

Innovation, R&D, and management of Intellectual Property Rights [IPR] are being included as a key factor for the success and survival of biotech business houses. Now, Business development and IPR are interlinked in many ways which include:

DEVELOPMENT in terms of intellectual capital of an enterprise;

OVERALL BUSINESS STRATEGY means Intellectual property and Innovation strategies as part of the agenda;

VISION regarding the importance of Intellectual property rights and its implementation;

INVESTMENT in terms of intellectual property management, product development, and innovation; and

MARKET HOLD in terms of new products, competitiveness, and international expansion of IP.

Despite of many development stages and difficulties from invention to process or product prototyping and further product development to actual marketing product, intellectual property rights have a great impact on businesses and their competitiveness, success, and development.



PATENTS

Patents in biotechnological inventions exist since 19th century. One of the oldest biotechnological patents was granted in Finland on November 8, 1843 for 'A Novel Method for producing yeast cultures' and another for very famous 'Yeast Making Method' of eminent microbiologist Louis Pasteur on July 29, 1873 by the French Patent Office. Alizarin, a red dye was one of the oldest patents granted in 1869 to a commercial firm BASF.

After a long battle worldwide on patentability issues on biotechnology, now, biotechnological inventions are patentable under the Indian Patent Law with few exceptions:

A- The living entities of natural origin or discovery of such as animal, plant in whole or any part thereof are not patentable in India.

B- Terminator gene technology and microorganisms are not patentable in India. However, microbiological processes can be patented. Specifically, processes for producing new-microorganisms through genetic engineering and the products resulting out of this process.

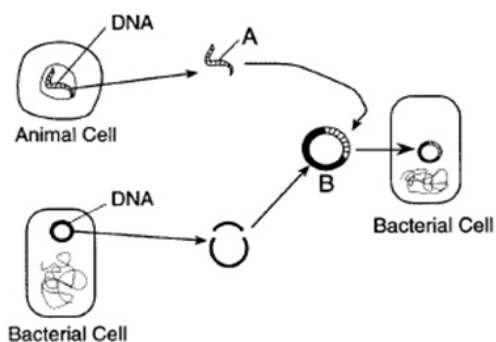
C- The biological materials such as organs, tissues, viruses etc and process of preparing the same are not patentable in India. But biotechnological materials such as recombinant DNA, plasmid and process of manufacturing thereof are patentable. A cell line is patentable if artificially produced.

D- Gene sequences, DNA sequences without having disclosed their function are not patentable. But, if the end result is non-living then R-DNA, RNA, Amino Acids are patentable subject to other provisions in the law.

E- The process of cloning human being or animals is not patentable. But, invention on Hybridoma Technology is patentable except protoplast fusion.

CASE STUDY

Recombinant DNA Technology



DEVELOPED BY: Stanley Cohen and Herbert Boyer in 1973

CONCEPTION OF IDEA: The idea for the gene cloning technique first arose in November 1972 at a scientific meeting on plasmids in Honolulu.

WORK: By early 1973, they launched on a series of experiments resulting in a method to select and replicate specific foreign genes in bacteria.

In 1974, Niels Reimers, a Venture Capitalist read in the New York Times about a new technique called "gene splicing" invented by them. He recognized that this was likely to offer a promising licensing opportunity, and approached the inventors to let him try to patent it.

In 1975, Cohen wrote an article for *Scientific American* explaining the DNA cloning technique. He emphasized its usefulness to basic science and also its commercial aspect for synthesizing antibiotics, hormones, and enzymes.

PATENT STORY

The first patent was issued on December 2, 1980, after 6 years under review at the U.S. Patent and Trademark Office. The original application was filed in November 1974.

The journey till grant was full of battles with strong opposition from society & US Government.

Niels Reimers, manager of Stanford's Office of Technology Licensing, had a large role in commercializing the patent and licensing of the cloning technology invented by Cohen and Boyer.

During that period Neils Reimers wrote "When I first went licensing, a lot of the companies, the business people, didn't really understand the technology".

Cohen-Boyer patent has become the gold standard for university technology licensing. How?

SUCCESS STORY

By August 1981, Stanford's OTL started offering special, non-exclusive licenses to the new recombinant DNA technology.

While there wasn't an immediate rush of interest, word spread through media coverage and Stanford's intensive marketing efforts.

By the deadline - midnight on December 15 - Federal Express trucks were lined up outside the doors to OTL.

When the deadline passed, 73 companies had signed agreements.

By the end of that fiscal year, August 31, 1982, license fees from the new DNA technology had produced over \$1.4 million as income to the applicants.

It is interesting to note that during the same period, all other technologies licensed by OTL together brought in just \$1.1 million.

Over the duration of the life of the patent (expired in December 1997), the technology was licensed to 468 companies.

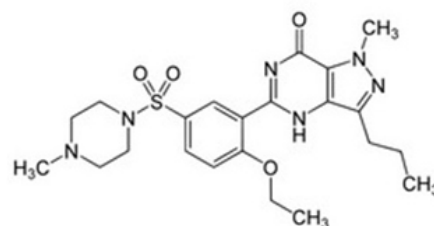


Commercial products developed by the licensees generated over \$35 billion through sales of recombinant DNA products over the life of the patent.

Stanford and the University of California generated \$255 million as licensing revenues.

Stanford reported 2,442 products based on recombinant DNA technique by the time the patent expired.

SILDENAFIL CITRATE



DEVELOPED BY: Peter Dunn and Albert Wood in 1994

CONCEPTION OF IDEA: The idea for the reverse erectile dysfunctions was discovered during the trial studies of Sildenafil as a heart medicine by Nicholas Terrett and colleague Peter Ellis in 1994 that it also increased blood flow to the penile region. The drug acts by enhancing the smooth muscle relaxant effects of nitric oxide, a chemical that is normally released in response to sexual stimulation.

WORK: Peter Dunn and Albert Wood, employees of Pfizer then worked on the crucial nine-step process to synthesize a Sildenafil (Viagra) compound into a pill. It was approved by the FDA on March 27, 1998, as the first pill to treat impotence.



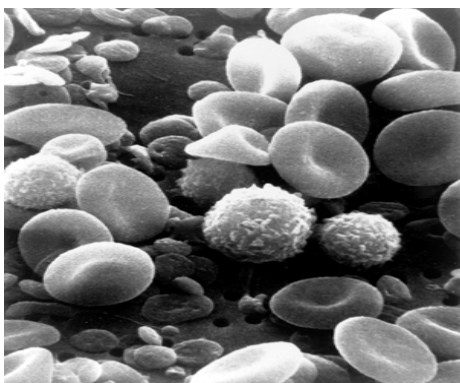
PATENT STORY

Sildenafil citrate was initially believed in curing high blood pressure and angina treatment. However, during Phase 1 trial angina trial reveals that it has one side effect of penile erections. Further, the Phase 2 clinical study shows only mild effect of sildenafil citrate blood circulation. Therefore, Pfizer decided to pursue its use for erectile dysfunction rather than for angina.

The drug was patented in 1996. US5250534 (Pyrazolopyrimidinone Antianginal Agents) filed on May 14, 1992 and US6469012 (Treatment of Erectile Dysfunction) filed on Mar 4, 1996 are listed in FDA for Viagra.

SUCCESS STORY

In first year of its production Viagra sales were made \$1 billion dollars. In 2000, Viagra sales accounted for 92 percent of the global market for prescribed erectile dysfunction pills. By 2007, Viagra's global share had plunged to about 50 percent due to several factors, including the 2003 market introductions of FDA-approved Cialis and Levitra, along with several other counterfeits and clones. However, it soon became a great success as annual sales of Viagra peaked in 2008 at US\$1,934 million. Pfizer's worldwide patents on sildenafil citrate will expire between 2011 and 2013.



SOME OTHER GREAT BIOTECH PATENTS

DNA Encoding an alpha-interferon (EP 32134): First Patent on human gene sequence granted in 1984 to Biogen.

Human Recombinant Erythropoietin (US 561024): Patent filed on Dec 13, 1983 that enables the industrial production of recombinant human erythropoietin (RhEpo) for treating anemia patients. In 1989, the U.S. FDA approved the hormone, called Epreo, which remains in use today.

Polymerase Chain Reaction (PCR, US 4683195): Granted on July 28, 1987 to Cetus Corporation. Later, Cetus sold the patent right to Roche for \$300 million in 1991. For this, inventor Kary Banks Mullis was awarded the Nobel Prize in Chemistry in 1993 for this great contribution in the field.

Hepatitis C Virus (EP 318216): Great Michael Houghton, from the University of Alberta had discovered the single strain of the virus to draw out broad cross-neutralising antibodies against all the different major strains.

Dolly the Sheep (EP 849990, Method for Cloning Animal): Dolly the sheep, has won the first UK patents for cloning. The California-based Geron has sole rights to the technology which he bought from Roslin Institute in Scotland where Dolly was created for \$45 million.

The Indian biotechnology company Shantha Biotechnics is credited as launching in 1997 India's "first domestically produced and marketed recombinant DNA product," Shanvac-B, a Hepatitis B vaccine.

Biocon, currently on top among all companies generating biotechnology revenues in India, has developed a "proprietary process" for manufacturing its recombinant human insulin product, Insugen.

Table-1: 9th BioSpectrum-ABLE listing of Top 10 BioTech Companies 2010-11

Revenue Rank	Company	Products
1.	Biocon	Recombinant human insulin
2.	Serum Institute of India	Recombinant Hep-B vaccine; Antisera
3.	Panacea Biotech	Vaccines
4.	Nuziveedu Seeds	Hybrid Seeds
5.	Reliance Life Sciences	Plasma Protein & API
6.	Quintiles India	Drug Development & Clinical Trial
7.	NovoNordisk	Insulin
8.	Rasi Seeds	Bt cotton hybrid seeds
9.	Mahyco	Bt cotton hybrid seeds
10.	Transasia	Molecular Diagnostics

PATENT LANDSCAPE

In last 7 years, the biotech industry is highly active in protection of its IP and doing extensive research and development to overcome the current competitive market force. The following data is just an overview of this activity in terms of Indian patent filing trend of these companies:

Sl. No.	Company	Patents	
		Published	Granted
1.	Biocon	60	49
2.	Serum Institute of India	31	9
3.	Panacea Biotech	124	31
4.	Nuziveedu Seeds	0	0
5.	Reliance Life Sciences	70	32
6.	Quintiles India	1	
7.	NovoNordisk	283	76
8.	Rasi Seeds	-	-
9.	Mahyco	7	1
10.	Transasia	31	1
11.	Aventis Pharma	229	127
12.	Indian Immunologicals	7	4
13.	Bharat Serums	12	6
14.	Advanced Enzyme Technologies	8	6
15.	LifeCare Innovations	10	3
16.	Strand Life Sciences	3	0

Source: Indian Patent Office Database

RECENT ACTIVITIES IN BIOTECH FIELD

World patent filing trends show a remarkable shift in biotech innovations. As of result of which new and advanced technologies are being introduced day by day to improving our living standard as well as minimizing the risk of vulnerable diseases. Innovators from around the globe are now very active in developing and filing of patent applications on new method and product related to the biotech field. Some of these activities are identified in specific biotech fields which are given below:

MAP KINASE	COMPUTATIONAL DESIGN	PROTEIN ENGINEERING	MEDICAL DEVICES
GYNECOLOGICAL SURGERY	ASSISTED ROBOTIC SURGERY	EXPRESSION SYSTEM	BACULOVIRUS
BIOFILM	ULTRAFILTRATION MEMBRANE	NUTRACEUTICALS	BIOACTIVE PEPTIDES
HYBRID MATERIALS	PLANT GROWTH PROMOTION	MEMBRANE BIO REACTORS (MBR)	BIOLOGICAL CONTROL AGENTS
GLYCOSIDE PREPARATION	RECOMBINANT PROTEINS	STEM CELLS AND REGENERATIVE MEDICINE	INTRA OPERATIVE COMPLICATIONS
POSTOPERATIVE COMPLIANCE	SURGICAL OUTCOME	HOLLOW SILICA NANO-PARTICLES	CONTROLLED RELEASE
TARGETED DELIVERY	DRUG DELIVERY	HEAVY METAL CONTAMINATION	HEMATOPOIETIC STEM CELL
EMBRYONIC DEVELOPMENT	ACCUMULATION	ENVIRONMENTAL CONTAMINATION	PHYTO-REMEDICATION
LAPAROSCOPY	VACCINE	MAMMALIAN CELL	BIOPOLYMER





CONCLUSION

Though, Indian Biotech Industry are generating revenues from generic version of invented products and processes of other countries, still they are gradually pacing up with innovation regime. Since product patent has implemented recently (in 2005) in India, we are now moving ahead from new and improved manufacturing process to the development of new and innovative biotech products.

Keeping in mind that IP has great role in the development and proliferation of an organization, Indian Biotech Companies taking all care to protect their IP in India as well as foreign countries. And, the time will come where Indian Biotech Industry will be known for 'Low Cost Quality Biotech Products Producers' in the world.



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